MIM/TDR AMDR Network Proposal Finalization Workshop
Host: Malaria Research Group Ibadan Nigeria

February 5th – 12th, 2002

Site: International Institute for Tropical Agriculture (IITA, Ibadan)

A workshop was held February, 2002, to finalize a proposal for the proposed network. This proposal would be presented to the MIM Task Force in March, 2002 at their annual meeting holding in Entebbe, Uganda.

PI and Co-PI were invited to this meeting (Ghana – Drs Kojo Koram and Abraham Oduro; Mali, Drs Abdoulaye Djimde and Jean Bosco Ouedreago; Nigeria, Drs. Shola Gbotosho and Catherine Falade; Tanzania, Mr. Kefas Mugittu and from Uganda, Dr Fred Kironde. From TDR/RCS was Professor Ayo Oduola, Dr. Olumide Ogundahunsi and MIM/TDR AMDRN Manager Dr. Wilfred Mbacham

Objectives of the workshop were as follows:

- Agreement to collaborate by establishing common protocols and by submitting a joint proposal.
- The investigators would agree to develop a common database and web-based system of management
- To have a status report of progress made so far of each site by April 28 – May 4th at the team building meeting in Scotland.

Researchers worked in groups to improve on the protocols and on the finalization of the proposal with two reference documents emerging - The SOPs and a Network Proposal:

The Network Proposal
The MIM/TDR AMDRN proposes to build adequate capacity in using targeted research to provide pertinent and timely data on *P. falciparum* resistance to national malaria control programmes for evidence-based policies on anti-malarial treatment.

Specifically the ADRN hopes to:

- Systematically define the characteristics of *Plasmodium falciparum* resistance to selected antimalarial drugs including Chloroquine, Amodiaquine, Sulphadoxine/Pyrimethamine(SP), Mefloquine, Halofantrine & Artesunate/SP combination.
- To obtain complete clinical, parasitological and pharmacokinetic data in children treated with the first line antimalarial drug in each study site of the network
- To obtain complete clinical parasitological and pharmacokinetic data on children treated with recommended second line drugs at each of the participating sites.
- Determine the current levels of *P. falciparum* resistance to the selected antimalarial drugs *in vitro* at the participating sites.
- Strengthen the capability of scientists to address the problem of drug resistance in malaria in Africa using targeted research as a vehicle for capacity building.

Study Design:
The network will use four parameters in the investigation of anti-malarial drug resistance and will study the association between clinical response to anti-malarial drugs, markers of drug resistance, *in vitro* drug susceptibility and anti-malarial drug levels in Africa through a collation of data collected from the network sites. This will be achieved by:

1) Using four parameters Clinical response, *in vitro* susceptibility testing (with elevated $1C_{50}$), blood / plasma levels of drugs in treatment failure cases by HPLC and molecular markers of drug resistance to establish a database of drug resistance malaria in Africa.
2) Continuing capacity building at the sites through human resource and infra-structure development.
3) Generating and analysing site specific data on patterns of anti-malarial resistance, useful for the formulation of rational anti-malaria treatment policies.

The Standard Operating Procedure
Purpose of the Guidelines:
These guidelines are designed in order to establish standard and common protocols to be used by all sites of the network. It provides detailed description of protocols for evaluating the four criteria of antimalarial drug resistance compiled after consultations with experts in the field. Each partner in the network has opportunity to review and contribute to the protocol and thus share the responsibility of accepting and conducting the studies in accordance with the guidelines. Verification of the pre-established facilities (clinical, laboratory, personnel) on-site, systematic written procedures for the conduct, data collection, documentation and verification of studies are necessary to ensure the validity of the data obtained, and subsequently the integrity of conclusion(s) drawn from the studies.

The guideline is divided into four parts in compliance with the four major criteria:

- *Part-I:* Guidelines for protocols involving clinical assessments of antimalarial drug resistance (clinical evaluation).
- *Part-II:* Guidelines for protocols involving *in vitro* susceptibility test.
- *Part-III:* Guidelines for protocols involving antimalarial drug level determination (analytical technique)
- *Part-IV*: Guidelines for protocols involving molecular markers. For identifying antimalarial drug resistance genotype and molecular markers of multiplicity of *P. falciparum* infections.

Effort in the first 12 months of the network will focus on the following **specific objectives**:

- Acquisition of complete clinical, pharmacokinetic, parasitolgical and molecular markers data on 150 – 200 patients treated with the first line antimalarial drug in each study site of the network.
- Acquisition of complete clinical, pharmacokinetic, parasitolgical and molecular markers data on 100 patients randomised into 2 groups to receive the rescue drug recommended in the study site and one other drug chosen from the list of potential alternative antimalarial drugs including Amodiaquine, Mefloquine, Halofantrine, Sulphadoxine / pyrimethamine (SP) or Artesunate / SP combination).

A technical team assisting the network manager will facilitate implementation of the protocols. The network manager will be responsible for quality assurance and coordination of the task force. The Malaria Research Reagent Resource center (MR4) will assist the network in provision of standard reagents and validation of protocols. Other organizations

including US National Library of Medicine (NLM) and South African Bioinformatics Institute (SANBI) will be enlisted to assist in communication and data management.

The Workshop was interspersed with Scientific talks by Mr. Lanre Bello and Ms Badru respectively on the data base and Modeling of anti-malaria drug resistance

Acknowledgements
The Ibadan Malaria research Group must be congratulated for their efforts in organizational details and for their hospitality. The students and all staff were so helpful in facilitating arrival and take off from the airport and in arranging for food.

Wilfred Mbacham, Manager